

moiety of lipid II, ramoplanin is thought to form a dimeric complex with the sugar moieties of lipid II on the outside of the bacterial cell wall (Hu et al. 2003).

2.1.4 Marine Life

Conotoxins

The conotoxins are the first group of natural products from marine life to be developed and approved as a drug. Originally isolated from marine cone snail species *Conus magus* (McIntosh et al. 1982), the conotoxins are a group of neurotoxic small peptides which contain a high amount of disulfide bridges. It was found that there are five distinct groups of conotoxins, namely, the α -, δ -, κ -, μ -, and ω -conotoxins, all targeting different receptors in the central nervous system (Olivera and Cruz 2000).

Although all of these conotoxins have interesting biological applications, only one specific ω -conotoxin, MVIIA (**20**, Fig. 10, ziconotide), a peptide 25 amino acids long which contains three disulfide bonds, has so far been developed and approved after clinical trials as an analgesic. Its total synthesis was achieved by using solid-phase peptide synthesis (Olivera et al. 1987).

Ecteinascidin-743

Ecteinascidin-743 (**21**, Fig. 11) is a marine natural product isolated from sea squirt species *Ecteinascidia turbinata* (Sigel et al. 1969). It is a potent cytotoxic agent which has been approved in 2007 for the treatment of soft tissue sarcoma. It exerts its mechanism of action through the binding to the minor groove in the DNA double helix and subsequently inducing double DNA strand breaks while preventing repairs through an unknown mechanism (Nicolaou and Montagnon 2008).

Structure elucidation of the active components of the extracts was achieved in 1990, where it was shown that ecteinascidin-743 had the highest potency (Wright et al. 1990; Rinehart et al. 1990). Soon after the structures were available, the total synthesis was achieved (Corey et al. 1996; Martinez and Corey 2000), and a semisynthetic approach that used the antibacterial natural product cyanosafractin

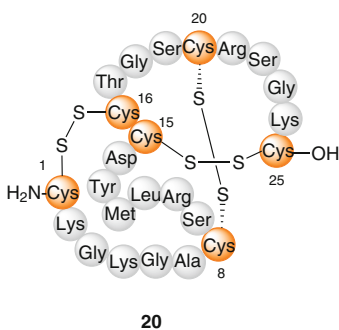


Fig. 10 Amino acid sequence of ω -conotoxin MVIIA (**20**). Disulfide bridges between Cys1–Cys16, Cys8–Cys17, and Cys15–Cys25 are drawn